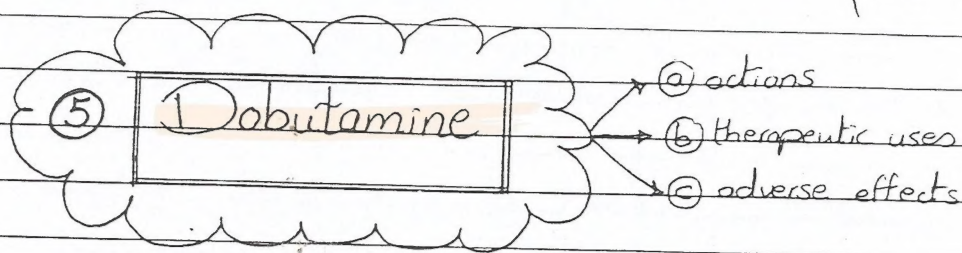


* بصورتها يا شباب احنا المرة الى فاتت اتكلمنا مع بداية ال Sympathetic وكنا بيأنا في ال Adrenergic agonists بس كنا مكملنا هسبي كنا اخذنا ال epinephrine وال norepinephrine وال dopamine وال isoproterenol.

* مهم جداً ال isoproterenol له اسم ثاني مهم هو isoprenaline نساها هسبي يقول انه احنا بنعطي المعلومات لنفسنا واللام الخرب الى احنا بنسحقه ده

* المرة دي هنكمل ال Direct Adrenergic agonist واولهم :



a) Actions :

- * it's a synthetic, direct acting catecholamine
- * it's a selective β_1 agonist
- * So it \uparrow Cardiac output \rightarrow have very few vascular effects

b) Therapeutic uses :

- * \uparrow Cardiac output in case of congestive heart failure with little \uparrow in heart rate
- * doesn't elevate oxygen demands of myocardium which is a very

important advantage over other sympathomimetic drugs

HR من يمس يا جيبى من الوقتى أنا زودت ال COP من يس ما أنزود ال

أرى

من يبقى أكبر أنا زودت ال stroke volume

$$COP = stroke\ vol \times HR$$

لأنه ال

من المهم إن ال HR زادت بنسبة قليلة من ذلك مجود عضلة القلب

لم يزد أوى وهو ده اللى أنا عايزه على ال oxygen demand

لعضلة القلب نفسها مايزيس من وده طبعاً فى حالة إن أنا يكون

عنى مشكلة فى ال coronary arteries اللى بتجيب الدم وال oxygen لعضلة

القلب نفسها على شكل تنغنى وتشتغل

© Adverse effects

① should be used with caution in case of atrial fibrillation, as it ↑ the A.V. Conduction

يجب على ال fibrillation اللى فى ال Atria ما توصلش ال ventricles

تبقى مهيبة

② Tolerance may develop on prolonged use

③ other adverse effects like those of epinephrine may develop

Pray alot for US

Pl 11111111 000

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⑥ Phenylephrine

- a) actions
- b) uses
- c) adverse eff.

a) actions

- ① it's a synthetic, direct acting non catecholamine.
- ② Bind to (α) receptors, favours (α_1) more than (α_2)
- ③ So, it's a vasoconstrictor \rightarrow raises both systolic, diastolic blood pressure
- ④ it has no direct effect on heart but it induces reflex bradycardia when taken parenterally

يعني ايدك؟ آف من زيادة في ضغط الدم

يعني يا صبي يا بنت لما بتزور ال blood pressure في Plasma يا صبي
يا بنت مع طريق ال Baroreceptors في قاعها؟ ويخت ال CNS
فال CNS يبعث impulses ال heart مع طريق ال vagal nerve
يقول له اهدأ سرعة يا عم ال صبح نزل ال Blood pressure
في ال Bradycardia يعني reflex bradycardia

b) Therapeutic uses

- ① often used topically on nasal mucous membranes as nasal decongestant.
- ② in ophthalmic solution \rightarrow Causes mydriasis \rightarrow by radial M_3 contractn, \therefore it can respond again to light by constrictor M_3 contractn, \therefore this is called active mydriasis

II non Catecholamine

① phenyl ephrine

② methoxamine

③ clonidine

④ metaproterenol

I phenyl Ephrine (synthetic)

A Actn

- more potent $\alpha_1 > \alpha_2$
- Vaso Constriction
- \uparrow SBP \uparrow DBP

N.B has no Direct effect on heart but

\uparrow reflex brady Cardia when taken Parenterally

?? why

B Therapeutical use

- ① Topically \rightarrow nasal Congestant
 \rightarrow ophthalmic prep.
To make Active mydriasis

???

responsive to light
 \therefore not block for Constrictor Muscle

C Adverse effect

- ① hypertension
- ② Head ache
- ③ Cardiac irregularities

N.B phenyl ephrine is non Catecholamine
so resists CoMT.

إليه القرفه ده يا عميانت ما تتكلم عربي وتفهمني

بعض يا عميانت عنك نوسم من ال Muscles في ال eye

① radial M_s → او حبلها contract_α بال (α) → Mydriasis

② constrictor M_s → كنا آختنا في ال Parasymp. Syst → لما يتفرق العصب

لضوء قوي → ال constrictor M_s بيحبلها contract_α فيتحلل Mydriasis

كده → ال Mydriasis اللي بيحبل لل eye في الأول بتسمى **active**

لضوء لما يتفرق للضوء بي respond

Blocker أنا لو حبل Mydriasis عم طريقه إنا أنا

ال receptor يتاع ال constrictor M_s فيحبلها relaxat_α → ويح

كده جيت عرفت ال eye للضوء → ال constrictor M_s بيحبلها

Blocker → فالضوء من هيات عليها فيس في respond

لضوء → كده بتسمى ال Mydriasis ده **passive Mydriasis**

يارب ركنه وصلت → او من فاهم تعالى لنا واحنا في بيوتنا

③ this drug is used to raise blood pressure in case of hypotension, to terminate episodes of supraventricular tachycardia (rapid heart arising from A.V. Junction, & atria)

Ⓒ Adverse effects:

- ① large doses can cause :
- * hypertensive headache
 - * Cardiac irregularities

V.T. N.B. → phenylephrine isn't a catecholamine derivative
∴ it's not a substrate for catechol-O-Methyl transferase (COMT)

Phenyl Ephrine \rightarrow (1) (2) methoxamine

• Synthetic

A Actn

- $\alpha_1 > \alpha_2$
- have no direct effect on heart but \uparrow reflex bradycardia

B Therapeutic uses

- ① III of hypotension during surgery \bar{e} halothane anesthetics
- ② relieve attacks of Paroxysmal Supraventricular Tachycardia

- Terminate episodes of Supraventricular Tachycardia

C Adverse effect

- hypertension
- Headach
- Cardiac irregularities

Direct

N.B Selective α_1 Agonist

- ① phenyl Ephrine
- ② Methoxamine
- ③ Me phentermine
- ④ Midodrine (prodrug)
 \downarrow
desally midodrine

N.B direct and indirect α_1 selective Agonist

Metaraminol

⑦ Methoxamine

بالضيق
phenylephrine

- ⊗ it's a synthetic, direct acting (α_1) agonist
- ⊗ used to ~~(relieve)~~ relieve the attacks of paroxysmal supraventricular tachycardia \rightarrow by reflex bradycardia i.e., (terminate episode of supraventricular tachycardia).
- ⊗ used to raise BP in case of hypotension during Surgery involving halothane anaesthetics.
- ⊗ There are other direct acting α_1 agonists as Mephentermine
- , others acting Both directly, indirectly as Metaraminol

⊗ Midodrine (Prodrug) $\xrightarrow[\text{body to}]{\text{converted in the}}$ desglymidodrine (direct acting α_1 agonist)

⑧ Clonidine

- ① it's a direct (α_2) agonist
 \rightarrow α_2 receptors mediate inhibitory action
- ② clonidine acts on (α_2) receptors in the CNS \rightarrow

3) Clonidine

- ① Direct α_2 Agonist (mediated inhibitory Actn)
- α_2 R found in CNS in vasomotor Center \rightarrow Inhibition \rightarrow vasodilation \rightarrow \downarrow PR \rightarrow \downarrow BP \rightarrow III of hypertension
 - \downarrow symptoms of Diaphoresis (hypertension)

4) metaproterenol

- Similar Isoproterenol But resist cut
- Act on β_2 R \rightarrow Bronchodilation
- so III of asthma & bronchospasm

N.B Selective β_2 Agonist

① terbutaline

② Albuterol

③ Salbutamol

③ it can minimize the symptoms that accompany the withdrawal of opiates or, Benzodiazepines
those symptoms are hypertension mainly.

⊛ although it resembles isoprenaline → But it's not a catecholamine
∴ it's resistant to COMT

⊗ it acts on B_2 receptors causing Bronchodilation, improvement of airway function, so used in asthma treatment → & reverse bronchospasm

* Terbutaline \rightarrow β_2 more selective agonist with longer duration of action \rightarrow Bronchodilator, reduce uterine contracting in Premature labor.

* Albuterol [Salbutamol] → the same as Terbutaline used as inhalant to relieve bronchospasm.

B indirect Acting Agent (indirect sympathomimetics)

- ↑ release of neurotransmitter from vesicles → effect
 - ↑ release of NE from presynaptic terminals (endogenous NE)
 - Don't act directly on post synaptic
- ex

① Amphetamine

- ↑ NE
- Act α → ↑ BP
- Act β → ↑ COP

- Abuse

- uses

- ① III of Depression
- ② " ~ Narcolepsy
- ③ Appetite Control

- C-I

in pregnancy

Teratogenic

② Tyramine

- not used clinically
- found in fermented food
- mainly oxidised by monoamine MAO

If patient ← MAO inhibitor →
↑ hypertension → Arrhythmia.

direct acting adrenergic agonists كل ال
يعتبر كل الحاجات التي يتدخل بها تسمى على ال receptors كطول وتعطل
ال effect كأنها Natural Neurotransmitter

ويعتبر هيدأ في ال indirect adrenergic agonists التي يتدخل على ال vesicles
وتزود ال release يتبع ال Natural neurotransmitter فتزود ال effect.

Indirect Acting Adrenergic Agonists

- * They Cause \uparrow of norepinephrine released from presynaptic terminals i.e., endogenous NE
- (But) \rightarrow they don't act directly on postsynaptic receptors.

They include :

Amphetamine

Tyramine

① Amphetamine

- * it acts by \uparrow release of catecholamines
 - $\therefore \uparrow$ BP by acting on α receptors
 - $\therefore \uparrow$ BP by \uparrow heart activity by acting on β receptors
- * it has CNS stimulatory effect \rightarrow is often mistaken by drug abusers

* it can be used in treatment of 8

① depression ② narcolepsy إحساس دائم بالنوم

③ appetite control ④ children hyperactivity من عارضة بمراقبة إزاي

* should be avoided during pregnancy due to its effects on fetus development i.e., teratogenic يجعل تشوهات في الجنين

② Tyramine

* it's not clinically used but found in fermented food as ripe cheese, wine.

* Normally, it's oxidized by MAO

→ if patient is taking MAO inhibitors → it can cause serious vasopressor episodes (vasoconstriction, → hypertensive crisis)

أزمة

أو متلازمة

أو متلازمة

Indirect adrenergic agonists لا يعملان مباشرة

Mixed adrenergic agonists agonists الـ و mixed

indirect. يعملان بشكل غير مباشر direct يعملان بشكل مباشر

Mixed acting Adrenergic Agonists

Ephedrine

Metaraminol

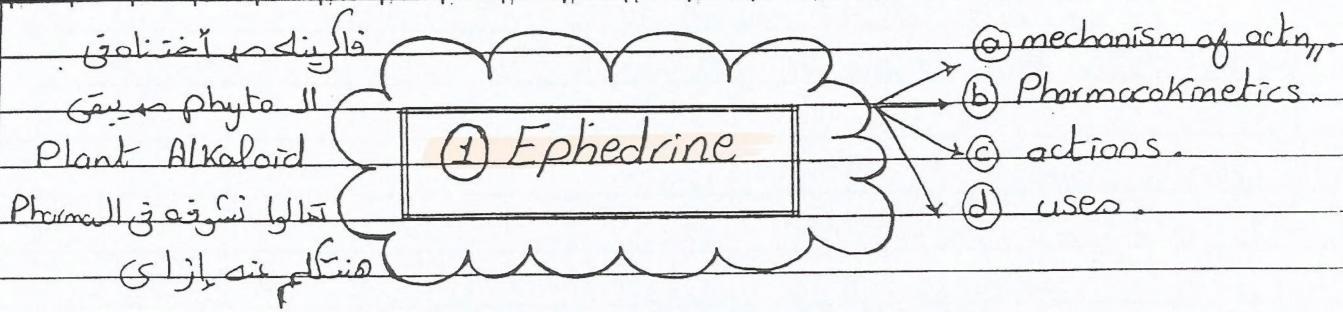
[C] mixed Acting Sympathomimetics

① Ephedrine

- A MoA
 - Direct → binds α, β
 - indirect → \uparrow NE release
- B Actn, Uses
 - \uparrow CO₂
 - +ve inotropic
 - +ve chronotropic
 - \uparrow SBP • \uparrow DBP
 - ① CNS stimulant (to fatigue - sleep)
 - ② \uparrow contractn of skeletal muscle + anticholinesterase in myasthenia gravis ???
 - ③ Bronchodilator → chronic asthma only why??? as prophylactic
 - ④ Improves athlete performance
 - ⑤ nasal congestant
- D pharmacokinetics
 - excellent absorbed orally
 - Penetrate BBB
 - resist MAO - GMT as they are noncatecholamine
 - eliminated unchanged in urine.

② Metaraminol

- like norepinephrine in Actn
- III of shock
- III of hypotension
- when NE, Dopamine I-V infusion is impossible?
- I-V as single dose
- mild vasoconstriction
- \uparrow CO₂ - \uparrow Activity of heart



① mechanism of actn., :

- ⊗ it can ↑ the release of catecholamines (NE) from presynaptic neurons
- ⊗ also it can Bind directly to α , β receptors
That's why we call it Mixed acting adrenergic agonist.

② Pharmacokinetics :

- ⊗ has excellent absorptn, orally
- ⊗ Penetrates BBB → reaches CNS
- ⊗ It's not a catechol ∴ not affected by COMT, MAO
∴ has longer duratn, of actn, than (NE)
- ⊗ Eliminated unchanged in urine as its not affected by COMT, MAO.

③ Actions :

- ① it ↑ both systolic, diastolic BP by ↑ vasoconstrictn, (α)
, ↑ cardiac stimulatr, (β)
- ② Mild CNS stimulatr, → ↑ alertness, ↓ fatigue, prevent sleep.

- ③ Enhances contractility, improves motor function, in Myasthenia gravis → especially if used with anticholinesterases

فأكثر الـ myasthenia gravis في كانت إليه ؟
 لا أكيد لا

في أفكاره في كانت حالة relaxatn, في الـ skeletal Ms
 كنت بتعالجها بأن أدوية anticholinesterases على أنه أزيد الـ Ach
 على الـ Neuromuscular Junction, فأزيد الـ contractility وأزيد الحركات
 الوعية

- ④ it produces Bronchodilation, But → it's less potent than epinephrine, isoproterenol in this effect, slower.
 ∴ it's just used prophylactically (الوقاية) in case of chronic asthma → to prevent attacks
 ∴ it's not used in acute asthma. → only chronic.

- ⑤ it improves athlete performance
 ∴ Banned in (olympic games) لأنه يمنع في الألعاب

d) Uses : استخدامات الـ actn

- ① used prophylactically in chronic asthma treatment.
- ② to raise blood pressure in cases of hypotension.
- ③ nasal decongestant → due to its local vasoconstrictor action.

But → the clinical use of ephedrine is ↓ due to presence of more potent drugs with fewer adverse effects.

* locally sympathomimetics

For nasal mucosal membrane, eye

- ex
1. oxy meta zoline
 2. xylometazoline
 3. propyl hexedrine

* orally sympathomimetics

For relief of nasal congestion

ex

- ↓
- ① phenyl Ephrine
 - ② pseud Ephedrine
 - ③ phenyl propanolamine

have same
pharmacological effect
of Ephedrine but
↓ CNS stimulation

suppress
Appetite &
mechanism
diff from
amphetamines

used as
OTC

risk of haemorrhagic
stroke ~~isobutyl~~

② Oral :

Some sympathomimetics have been used for relief of nasal congestion, such as :

- ① phenylephrine
- ② pseudoephedrine
- ③ phenylpropanolamine

Phenylpropanolamine

① has same pharmacological effect of ephedrine but with less CNS stimulation,

② suppresses the appetite but with mechanism different from that of amphetamine.

③ Used as an OTC drug
يعني يتصرف فيه غير رخصة
OTC = over the counter

④ it was found that it ↑ the possibility (risk) of haemorrhagic stroke (سكتة دماغية)

FDA issued نشرت a public warning about this risk

it manufacture, marketing is ↓

* دلوقتي حيتدي في حاجة جديدة خالص وهي ال Adrenergic antagonists

يعني بنا من نصيحتي مني من فاهات ال 13 صفحة جدول وحطهم على ال 20 صفحة بتوع المحاضرة اللي فاهات اللي كنا ابدينا فيهم ال adrenergic (pg 37-55) واعلم محاضرة لو حدها من كلام بيتكلموا عن موضوع واحد وهو ال adrenergic وال adrenergic agonist من وجه اول الصفحة القائمة له آخر المحاضرة من ذي محاضرة لو حدها من كلام بيتكلموا عن حاجة واحدة وهي ال Adrenergic antagonist من وجهت حاجة من نصيحتي من عليز تعمل بيها OK من نايز براحتكم من راحة الله